SCIENTIFIC ABSTRACT

This is a Phase I/II, open-label, single arm gene therapy clinical trial of AdV-tk + valacyclovir in combination with standard chemoradiation for newly diagnosed patients with inoperable, locally advanced pancreatic cancer. The rationale for this research is based on preclinical studies demonstrating local and systemic anti-tumor effects of AdV-tk/prodrug gene therapy combined with chemoradiation. The approach is further justified by the poor prognosis from current therapeutic approaches for pancreatic cancer. The primary objective for the Phase I component is to evaluate the safety of AdV-tk + valacyclovir in combination with standard chemoradiation for pancreatic cancer; for the Phase II, it is to evaluate clinical efficacy of the approach. The first phase of the trial will be a dose escalation with 3-6 patients per dose. Four dose levels of AdV-tk, ranging from $3x10^{10}$ to $1x10^{12}$ vector particles in half log increments, will be evaluated. Once the MTD is reached or the highest dose level is completed without significant toxicity, the trial will continue to accrue patients to a total of 40 evaluable patients at that dose level. Patients will receive the 1st dose of AdV-tk at the time of definitive diagnosis via endoscopic ultrasound intratumoral injection. Vector injections will be followed by 14 days of the oral prodrug valacyclovir. Standard radiotherapy and 5-FU will begin 24-72 hours after AdV-tk injection. A 2nd injection of equal dose will be administered to the tumor at the time of laparotomy for intraoperative radiotherapy.